Modeling Reactive Chemistry in Protein Active Sites

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Questions abound regarding the role of enzyme structure and active-site metal ions in controlling the outcome of catalytic reactions. The enzyme Rubisco, for example, catalyzes two competing reactions: carboxylation that leads to carbon fixation, and oxidation that leads to wasteful loss of carbon. Alterations in the enzyme active site structure and substitution of the active-site Mg2+ ion for other divalent ions shifts the relative rates of competing reactions, changing the specificity factor of the enzyme. In our efforts to model catalytic specificity, we apply a muilti-scale quantum/molecular mechanical approach. Our goal is to analyze and interpret the observed specificity ratios in terms of calculated structural, electronic, and thermodynamic quantities, thus gaining chemical insight regarding the protein active site as well as quantitative benchmark results for other modeling efforts. Here we present our current work on reduced models of the enzyme, various metal ions, and ion-enzyme complexes.

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